REMARKS/ARGUMENTS

Claims 20-27 are pending in the present case. Claims 20-27 as well as the species of Formula I are currently under examination. In order to expedite prosecution, claim 27 has been amended to set forth the proper name for the various adipogenesis marker genes recited therein. In addition, the Abstract has been amended so that it is more narrative in form and of a sufficient length. No new matter is introduced with either of these amendments.

Applicants acknowledge, with appreciation, the Examiner's indication that the drawings submitted August 21, 2007 and December 18, 2007 are accepted.

In the Office Action, the IDS was objected to as allegedly failing to comply with 37 C.F.R. §§ 1.97, 1.97 and MPEP § 609 for failing to provide English translations of cited references, and the Abstract was objected to as being of insufficient length. In addition, claim 27 was rejected as allegedly indefinite. Finally, claims 20-27 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. For the reasons set forth herein, each of these objections/rejections is overcome.

Information Disclosure Statement (IDS)

In the Office Action, it is alleged that the IDS filed June 8, 2007 fails to comply with 37 C.F.R. §§ 1.97, 1.97 and MPEP § 609 because no English translation was provided for references FR 2793794, PCT Publication No. WO 02/0518843 and PCT Publication No. WO 00/71543.

In order to expedite prosecution, Applicants submit concurrently herewith a Supplemental IDS making U.S. Patent Nos. 7,122,669 and 7,041,824 of record. It is noted that the subject matter disclosed in U.S. Patent No. 7,122,669 is cumulative to the disclosure of PCT Publication No. WO 00/71543 and its priority application FR 1999 06456, which published as FR2793794. In addition, the subject matter disclosed in U.S. Patent No. 7,041,824 is cumulative to the disclosure of PCT Publication No. WO 02/051843. It is believed that the filing of this Supplemental IDS overcomes the concerns raised by the Examiner. Applicants request that the Examiner now consider these cited references and sign-off on the Supplemental IDS.

Objection to the Abstract

In the Office Action, the Abstract of the present application was objected to as being of insufficient length. In an effort to expedite prosecution, Applicants have amended the Abstract so that it is more narrative in nature as so that it is of sufficient length. As amended, the Abstract recites:

> The present invention provides compounds, compositions and methods for dedifferentiating lineage committed mammalian cells into multipotent stem cells. The present invention also provides methods of inducing dedifferentiation of lineage committed mammalian cells into multipotent stem cells, which can be further differentiated into various lineage committed cells. Methods of identifying additional compounds useful for inducing dedifferentiation of lineage committed cells into multipotent stem cells are also provided.

In view of the amendment to the Abstract, the concern raised in the Office Action is overcome. Accordingly, Applicants request that this objection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 27 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In making this rejection, the Office Action states that the use of the terms "ob," "Ucp," "PPARγ," "C/EBPs" in claim 27 is unclear. The Office Action, however, indicates that this rejection can be overcome by spelling out each of these terms.

In order to expedite prosecution, Applicants have amended claim 27 to recite the full name for each of the adipogenesis marker genes recited therein. As amended, claim 27 now recites:

> 27. The method of claim 25, wherein the adipogenesis marker gene is selected from the group consisting of: obsese (ob) gene, uncoupling protein (Ucp) gene, peroxisome proliferator-activated receptor γ (PPARγ) gene and CCAAT/enhancer-binding proteins (C/EBPs) genes.

In view of the amendment to claim 27, the Examiner's concern is overcome. Accordingly, Applicants request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 20-27 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirements. For the reasons set forth below, Applicants respectfully submit that the specification, as filed, provides more than adequate support and enablement for the instant claims in the manner provided by 35 U.S.C. § 112, first paragraph.

A particular claim is enabled by the disclosure in an application if the disclosure, at the time of filing, contains sufficient information so as to enable one of skill in the art to make and use the claimed invention without undue experimentation. *See, e.g., In re Wands*, 8 USPQ2d, 1400 (Fed. Cir. 1988); *see also,* M.P.E.P. § 2164.01. Even if complex or extensive experimentation is required to practice the invention, such experimentation does not necessarily mean that the invention is not enabled. Complex experimentation is not necessarily undue, if the art typically engages in such experimentation. *See,* M.P.E.P. § 2164.01. A considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *See,* M.P.E.P. § 2164.06. A rejection for undue breadth is inappropriate where "one of skill could readily determine any one of the claimed embodiments." *See,* M.P.E.P. § 2164.08.

The claimed invention is directed to a method for identifying compounds (such as 2,6-disubstituted purines) that induce dedifferentiation of lineage committed mammalian cells into multipotent stem cells. In this method, a lineage committed mammalian cell (such as an adipocyte, a myoblast, an osteoblast, a chrondrocyte, *etc.*), is contacted with a test compound suspected of inducing dedifferentiation of lineage committed cells. Thereafter, the cells are cultured in a first cell culture media that induces differentiation of the multipotent stem cell into a first cell type and in a second cell culture media that induces differentiation of the multipotent stem cell into a second cell type. It is then determined whether the cells have undergone

differentiation into the first or second cell type, wherein induction of differentiation into both the first cell type and the second cell type identifies the test compound as a compound that induces dedifferentiation of lineage committed mammalian cells.

Applicants respectfully submit that the specification is fully enabling for a method of screening a compound for its ability to dedifferentiate a lineage committed mammalian cell to its multipotent progenitor stem cell. As the Examiner has pointed out, the specification provides a detailed description of this process for myoblast cells (*see*, Examples 2-4). These examples unequivocally demonstrate that the presently claimed method can be used to identify compounds that induce dedifferentiation of lineage committed mammalian cells into multipotent stem cells. Applicants respectfully submit that one having ordinary skill in the art could readily adapt this screening method to begin from any number of other lineage committed mammalian cells, such as osteoblasts, adipocytes, chrondrocytes, *etc.* In fact, it has been found, for example, that Reversine, which is a 2,6-disubstituted purine falling within the scope of Formula I, has been found to dedifferentiate adipogenic and osteogenic lineage-committed cells and to reprogram fibroblasts to increase their plasticity (*i.e.*, to enable them to differentiate into muscle, bone, fat and cartilage cells).

In support of this non-enablement rejection, the Examiner makes reference to pluripotent stem cells and alleges that there are "dramatic molecular and cellular differences between human and mouse embryonic stem cells," citing Allegrucci *et al.* as supporting the position that "there is difference in pluripotency marker molecules, transcriptional profiling, genetic stability and epigenetic stability even among different human embryonic stem cell lines" (*see*, pages 7 and 8 of the Office Action). However, the currently pending claims are directed to mulitpotent stem cells, not pluripotent stem cells. Moreover, it is clear from a reading of the specification that dedifferentiation of the lineage committed mammalian cell into a multipotent stem cell can be identified, *e.g.*, by detecting the loss of expression of a marker gene expressed by the lineage committed mammalian cell.

The Examiner also alleges that "the differentiated first and second cell types must be lineage correlated to the lineage committed mammalian cells exposed to the test compound such that differentiation of a multipotent stem cell into both first and second cell types could be

used as an indicator that said test compound is a compound that induces dedifferentiation of lineage committed mammalian cells" *see* page 10 of the Office Action). Applicants respectfully ***disagree***.

Lineage committed mammalian cells such as adipocytes, myoblasts, osteoblasts, and chondrocytes are all of mesenchymal lineage and are derived from the mesoderm. Dedifferentiation of any of these lineage committed mammalian cells results in a multipotent stem cell. Multipotent stem cells have the ability to differentiate into various lineages of cells, including transdifferentiation. For example, multipotent stem cells of the mesenchymal lineage, such as bone marrow stem cells, hematopoietic stem cells, or mesenchymal stem cells, can differentiate into adipocytes, myoblasts, osteoblasts, and chondrocytes (all of which are derived from mesoderm). Additionally, multipotent stem cells of the mesenchymal lineage have been shown to transdifferentiate into neurons (derived from the ectoderm). Further examples of transdifferentiation include the differentiation of precursor or progenitor cells (*i.e.*, stem cells) pre-committed to cell types of one lineage that can differentiate into specific cell types of another lineage, *e.g.*, pre-adipocytes transdifferentiate into osteoblasts or myoblasts transdifferentiate into osteoblasts.

Finally, the Examiner further alleges "that the test compound is the compound that induces differentiation of multipotent stem cells into a first and a second cell type, therefore, the test compound should be a 'differentiation' compound rather than a 'dedifferentiation' compound" (*see*, page 11 of the Office Action). Applicants respectfully ***disagree***.

Again, the pending claims are directed to "a method for identifying compounds that induce dedifferentiation of lineage committed mammalian cells into multipotent stem cells" (*see*, *e.g.*, claim 20). As set forth in the specification and as understood by those of skill in the art, "dedifferentiation" refers to the process by which lineage committed cells (*e.g.*, myoblasts, osteoblasts, adipocytes, chrondrocytes, *etc.*) reverse their lineage commitment and become precursor or progenitor cells (*e.g.*, multipotent stem cells), which can then be differentiated into a variety of different lineage committed cell types. Thus, a lineage committed cell contacted with the test compound and that is capable of differentiating into first and second cell types ***indicates that the test compound has dedifferentiated the lineage committed cell into a multipotent stem***

cell. Again, this is because a lineage committed cell will not differentiate into cells of more than one lineage unless it has first been dedifferentiated.

In contrast to the test compound and as recited in the claims, the first and second cell culture media induce the "differentiation" of the multipotent cell into first and second cell types, respectively. Thus, the claims as filed are, in fact, correct in referring to the test compound as a "dedifferentiating compound" if the test compound is capable of inducing dedifferentiating of lineage committed mammalian cells.

In view of the foregoing, Applicants respectfully submit that the specification, as filed, provides more than adequate support and enablement for the instant claims in the manner provided by 35 U.S.C. § 112, first paragraph. Accordingly, Applicants urge the Examiner to withdraw the rejection under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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